Nontechnical Abstract

Despite considerable advances in understanding the causes of cancer and in the development of improved treatments, there has been no overall reduction in cancer mortality for the majority of patients with cancer that has spread beyond the original site (metastatic disease). For patients with metastatic melanoma, no treatments can cure the cancer and treatment does not result in prolonging life. Patients with melanoma that spread throughout the body generally live on average only 8-9 months. For women with metastatic breast cancer, chemotherapy and hormonal therapy offer a chance for improved symptoms but almost no opportunity for cure. New approaches for the treatment of metastatic breast cancer and metastatic melanoma are clearly needed. Strategies that use the immune system to target tumor cells are attractive. Much has been learned over the past 15 years in the way the immune system works, what is required for the immune system to recognized cancer cells as different from self or normal cells, and ways to stimulate a specific immune response to cancer cells while sparing most normal cells.

The goal of this project is to test in a clinical trial whether injection of tumor nodules with a virus carrying a gene called B7-1 will stimulate an immune response against the tumor cells and that that immune response, usually T cells, will be able to kill cancer cells. The B7-1 gene helps the immune system to recognize the cancer cells which normally do not have this protein on the cell surface. The viral carrier (vector) brings the B7-1 gene into the cancer cells. The B7-1, now on the cancer cell can be thought of as a red flag on the surface of the cancer cells, alerting and waving down important immune fighting cells.

We will evaluate the safety and feasibility of treating patients with metastatic breast cancer and metastatic melanoma by tumor injections of an virus containing the human B7-1 gene. In the clinical trial, patients with incurable, advanced cancer who have accessible tumors (on the skin or lymph nodes) will be injected with the virus containing the B7-1 gene. The overall objectives of this study are to assess the local and systemic toxicity associated with treatment. Correlative laboratory studies will be conducted which will assess the immunologic effects of treatments well as the success and duration of gene transfer.

In this study three doses of virus will be tested. The starting dose was chosen for its apparent safety from animal studies. At least 2 tumor sites will injected. Four patients will be treated at each dose level. Patients will be monitored closely for side effects related to therapy. Sequential tumor biopsies of treated and untreated sites will be performed to access whether the gene (B7-1) was successfully transferred and to test if a specific immune response developed against the patients own cancer. Tumor shrinkage will also be evaluated after therapy.